UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,754	09/01/2006	Yoshiko Yoshiyama	2006_1459A	3249

513 7590 08/17/2009

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
08/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,754	YOSHIYAMA ET AL.	
	Examiner	Art Unit	
	JAE W. LEE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-13 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 8-13 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/29/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

The previous amendment to claims, filed on 05/27/2009, is acknowledged, wherein Applicants have canceled claims 6, 7 and 14-17, and amended claims 8-10 and 18-20.

Claims 1-5, 8-13 and 18-20 are pending in this application.

Priority

The instant application is the 371 national stage entry of PCT/JP05/03508, filed on 03/02/2005. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application JAPAN 2004-057373 filed without the English translation on 03/02/2004.

Election

Applicant's election of Group I, claims 1-5, 8-13 and 18-20, drawn to a method of producing a cell extract or a protein for cell-free protein synthesis in the reply filed on 05/27/2009 is acknowledged. Because applicant did not distinctly and specifically point

out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/29/2006 is acknowledged. All of the references cited therein have been considered by the examiner.

Claim Objections

Claims 3, 11 and 13 are objected to because of the following informalities:

Claims 3 and 11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 3 and 11 recite "wherein the affinity support carries a substance which can bind to the protein synthesized using the cell extract for cell-free protein synthesis produced by the method according to claim 1 [or 2]". However, the noted phrase fails to further limit claim 1 or 2

because by the virtue of being an affinity support, it must carry a substance which can bind to the protein synthesized using the cell extract for cell-free protein synthesis according to claim 1 or 2.

Claim 13 is objected to for being duplicative of claim 4. The reason is that since claim 3, which claim 13 depends from, does not further limit the subject matter of claim 1 as noted above, claim 13 is duplicative of claim 4.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 8-13 and 18-20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2-5 and 8-13 dependent therefrom) is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step of producing a cell extract, i.e., culturing cells, disrupting the cell membrane and removing the cell membrane therefrom, thereby producing the cell extract.

Claims 9 and 10 recite the limitation "the obtained synthesis reaction solution" in claim 1. There is insufficient antecedent basis for this limitation in the claim. In the interest of advancing prosecution, the noted phrase is interpreted as “said cell extract”.

Claims 9 and 10 recite the phrase, "a cell extract for cell-free protein synthesis produced by the method of claim 1; and contacting said cell extract with an affinity support used in the production of the cell extract or with an affinity support which is substantially the same as the affinity support to allow the protein to bind to the affinity support" which is unclear and indefinite. The reason is that since the cell extract, produced by the method of claim 1, already contains an affinity support which can bind the protein, it is unclear how contacting said cell extract with "*an affinity support which is substantially the same as the affinity support*" after the fact that the protein is already to bound to the affinity support present in the cell extract as described in claim 1, allows for the purification of the protein or the interaction study of the protein. In the interest of advancing prosecution, the phrase, "or with an affinity support which is substantially the same as the affinity support" is not given any patentable weight.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: for instance, steps of adding a target substance into the cell extract, contacting the target substance with the protein, removing the affinity support and washing the affinity support in a condition suitable for determining whether the target substance is specifically bound to the protein or not.

Claims 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: for instance, steps of producing cell extracts having a protein synthetic activity, and adding an affinity support, having an

affinity to a protein to be synthesized, to the cell extracts, prior to the synthesis of the protein.

Claim 18-20 recite the limitation "wherein substances…" in claims 18-20, respectively. There is insufficient antecedent basis for this limitation in the claim. The reason is that the "substances" are never mentioned in claims 18-20 prior to the "wherein substances" clause, which refers back to "substances" and further defines the characteristics of the substances. In the interest of advancing prosecution, the phrase, "wherein substances…are removed from the cell extract" is not given any patentable weight.

Claims 19 and 20 recite the limitation "the obtained synthesis reaction solution with an affinity support used in the production of the cell extract" in claim 19 and 20, respectively. There is insufficient antecedent basis for this limitation in the claim. In the interest of advancing prosecution, the noted phrase is interpreted as "said cell extract with an affinity support".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Gonzalez et al. (A Novel Interaction between Perlecan Protein Core and Progranulin,

The Journal of Biological Chemistry, Vol. 278, No. 40, Issue of October 3, pp. 38113–38116, 2003).

The instant claims are drawn to a method of producing a cell extract for cell-free protein synthesis, comprising the step of contacting a cell extract having a protein synthetic activity with an affinity support having an affinity to a protein to be synthesized using the extract, and removing substances bound to the affinity support from the cell extract, and wherein the affinity support does not impair the protein synthetic activity of the cell extract when the affinity support is contacted with the cell extract; and a method of analyzing an interaction between a protein and a substance, comprising: performing protein synthesis reaction by using a cell extract for cell-free protein synthesis; and contacting said cell extract with the affinity support, which carry a target substance, to thereby analyze an interaction between the protein and the target substance (see above 112 2nd paragraph rejections for the claim interpretation).

Gonzalez et al. teach a method of analyzing an interaction between two proteins, Perlecan Domain V and Progranulin, i.e., a protein and a target substance, comprising: performing protein synthesis reaction by the use of a cell-free TNT reticulocyte cell extract (commercially available kit from Promega); and contacting said cell extract with the anti-Myc or anti-HA antibodies combined with Protein A/G agarose beads, i.e., affinity support, thereby performing the co-immunoprecipitation assay, thereby analyzing the interaction between the proteins (see page 38113, right column, under "EXPERIMANTAL PROCEDURES - *In Vitro Transcription/Translation, Co-immunoprecipitation, and Immunoblotting*" and Figure 3 on page 38115). It is noted by

the Examiner that it is an inherent characteristics of the anti-Myc or anti-HA antibodies combined with Protein A/G agarose beads to not impair the protein synthesis of the cell-free *in vitro* translation reactions using TNT reticulocyte cell extract. Therefore, claims 1, 10 and 20 are anticipated by the teachings of Gonzalez et al.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 8, 9, 11-13, 18 and 19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Madin et al. (A highly efficient and robust cell-free protein synthesis system prepared from wheat embryos: Plants apparently contain a suicide system directed at ribosomes, PNAS, January 18, 2000, Vol. 97, No. 2, pp: 559–564) in view of Zacharias et al. (Recombinant-protein solubility screening using the EasyXpress in vitro translation system, QIAGEN News 2004 e6, Retrieved from the Internet <URL:www1.qiagen.com/literature/qiagennews/weeklyArticle/04_02/e6/default.aspx>).

The instant claims are drawn to a method of producing a cell extract for cell-free protein synthesis, comprising the step of contacting a cell extract having a protein synthetic activity with an affinity support having an affinity to a protein to be synthesized using the extract, and removing substances bound to the affinity support from the cell

extract, and wherein the affinity support does not impair the protein synthetic activity of the cell extract when the affinity support is contacted with the cell extract (see above 112 2nd paragraph rejections for the claim interpretation).

Madin et al. teach a method of producing a protein, i.e., DHFR via cell-free protein synthesis, comprising synthesizing said protein using cell-free wheat germ cell extract (see page 560-561 under "Materials and Methods").

Madin et al. do not teach a method of contacting said cell extract with an affinity support.

Zacharias et al. teach a method of producing a protein via cell-free protein synthesis comprising attaching His-6 tags to the protein of interest, using the cell-free *in vitro* translation reactions to express said protein, and contacting the reactions with an affinity support, i.e., Ni-NTA Magnetic Agarose Beads, which has an affinity to the His-6 tagged protein of interest, removing the said affinity support, thereby purifying the protein of interest (see pages 1-5). Since this is a commercially successful method of producing a protein of interest utilizing the Ni-NTA Magnetic Agarose Beads, i.e., a nickel immobilized support, it is an inherent characteristics of the Ni-NTA Magnetic Agarose Beads not to impair the protein synthesis of the cell-free *in vitro* translation reactions.

It would have been obvious to one of ordinary skill in the art to make and use a method of producing a protein of interest, i.e., DHFR, via cell-free protein synthesis, comprising [i] attaching His-6 tags to the protein of interest, [ii] synthesizing said protein using cell-free wheat germ cell extract as taught by Madin et al., [iii] contacting the cell

extract with Ni-NTA Magnetic Agarose Beads, i.e., an affinity support, which has an affinity to His-6 tagged protein, and are known not to impair the protein synthesis, and [iv] removing the Ni-NTA Magnetic Agarose Beads, thereby purifying the protein of interest. One would have been motivated to replace the cell-free *in vitro* translation kit taught by Zacharias et al. with the cell-free wheat germ cell extract taught by Madin et al. because Madin et al. teach that there are numerous advantages to use the wheat germ cell-free systems, i.e., [1] low cost, [2] easy availability in large amounts, [3] low endogenous incorporation, [4] the capacity to synthesize high-molecular-weight proteins, and [5] more suitable for the expression of eukaryotic proteins (see page 559, right column, 2nd paragraph). In addition, there is a high expectation of success because [A] wheat germ cell extracts in the cell-free protein synthesis, and [2] affinity tags/support for the purification of recombinant proteins have been rampantly practiced in the field of recombinant protein production/purification prior to the filing of the instant application. As discussed in KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385 (2007), it is considered obvious to combine prior art elements known to be used in equivalent fields of endeavor together into a single combination. The reference clearly shows that the method of using commercially available cell-free protein synthesis kit taught by Zacharias et al. and the method of using wheat germ extracts for cell-free protein synthesis were known to be used in equivalent fields of endeavor, i.e., in the field of cell-free protein synthesis; thus, it is considered obvious to combine them together. Therefore, Claims 1-5, 8, 9, 11-13, 18 and 19 are *prima facie* obvious over the combined teachings of the prior art.

Conclusion

Claims 1-5, 8-13 and 18-20 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on M-F between 10:30-7:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAE W LEE/
Examiner, Art Unit 1656

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656